Remarks

Claims 1, 117, 121, and 126-137 are pending. Claims 121 and 132 were amended to more clearly claim what applicants consider to be their invention. Claims 121 and 132 have been amended to require that the first nucleic acid cleaving reagents not be Type IIS restriction enzymes. This finds support at least on page 11, line 24, where it is indicated that Type IIS restriction enzyme need not be used, and page 16, lines 7-9, where non-Type IIS restriction enzymes are said to be preferred as the first nucleic acid cleaving reagent.

Applicants appreciate the indication that claims 1, 117, 126-131, and 133-137 are free of the prior art.

Double Patenting Rejection

Claims 1, 117, 121, and 126-137 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-131 of U.S. Patent No. 6,383,754. Applicants respectfully traverse this rejection.

Applicants are preparing and will submit a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c) relative to U.S. Patent No. 6,383,754 as soon as it is signed. It is believed that this will obviate the present rejection pursuant to M.P.E.P. § 804.02.

Rejection Under 35 U.S.C. § 102

Claims 121 and 132 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sapolsky et al. (U.S. Patent No. 5,710,000; "Sapolsky") in view of Jones (U.S. Patent No. 5,858,671). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claims 121 and 132 have been amended and now are drawn to a method of producing binary sequent tags in part by incubating a nucleic acid sample with a nucleic acid cleaving reagent that is not a Type IIS restriction enzyme. As indicated in the Office Action mailed May 21, 2003, this feature distinguishes the claimed method from the prior art. For at least this reason, claims 121 and 132 are not obvious in view of Sapolsky and Jones.

Claims 121 and 132 also require that one strand of the adaptor-indexers is covalently coupled to the nucleic acid fragments and that, after coupling, the adaptor-indexers remain fully or partially single-stranded. Thus, claims 121 and 132 do not require either covalent coupling or the **presence** of a complementary strand for the adaptor indexer.

Sapolsky discloses only the use of Type IIS restriction enzymes for the initial digestion. Sapolsky also fails to suggest the use of any other type of restriction enzyme for this step. A main point of the Sapolsky method is to generate an overhang in unknown sequences (so that those sequence can be "captured"). Because a restriction enzyme that cleaves within its recognition site (as, for example, Type II restriction enzymes do), such enzymes are not suitable for the Sapolsky method. This point is clearly recognized in Saplosky (see, for example, column 6, lines 3-6). Sapolsky also fails to disclose covalent coupling of only one strand of an adaptor nor that the adaptor remain fully or partially single-stranded.

Jones discloses ligation of an adaptor to a nucleic acid fragment. Jones fails to disclose or suggest use of a non-Type IIS restriction enzyme in a method such as that of Sapolsky. Jones was cited as teaching that adaptors can be added one strand at a time. Jones states that: "One or both strands of an adaptor can be ligated, or one or both ends of a single-strand hairpin adaptor

can be ligated. Also, one strand of an adaptor can be ligated followed by hybridization, without ligation of the complementary strand, to generate a double-stranded recognition domain." See column 38, lines 50-55. Significantly, Jones fails to disclose or suggest leaving the adaptor fully or partially single-stranded as required by claims 121 and 132. Thus, Jones fails to disclose or suggest this aspect of claims 121 and 132. For at least these reason, Jones fails to provide the teachings missing from Sapolsky.

Because Sapolsky and Jones fail to disclose or suggest at least one feature of the present claims, Sapolsky and Jones fail to make obvious the claims. Accordingly, for at least this reason, claims 121 and 132 are not obvious in view of Sapolsky and Jones.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

No fee is believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Robert A. Hodges — Date: 8/21/2003